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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER

HSU, G

ART UNIT

PAPER NUMBER

1627

DATE MAILED:

02/29/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary

Application No.

09/167,351

Applicant(s)

Haaf et al.

Examiner

Grace Hsu, Ph.D.

Group Art Unit

1627



☒ Responsive to communication(s) filed on Jan 18, 2000

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire three (3) month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-15 is/are pending in the application.

Of the above, claim(s) 10-15 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-9 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☒ received in Application No. (Series Code/Serial Number) 60/061,619.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

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DETAILED ACTION

1. Claims 1-15 are pending in the above-identified application.
2. Claims 1-9 are under examination.
3. The Response to Restriction Requirement received on January 18, 2000 has been received and entered as Paper No. 6.
4. The above-identified application derives priority from U.S. Provisional Application No. 60/061,619, filed October 9, 1997, now expired, and from Federal Republic of Germany Application No. 197 45 628. 6, Filed October 10, 1997.

Election/Restriction

5. Applicants' [a] election of Group I, claims 1-9, with traverse, drawn to a process of preparing chemical compounds of formula (I); and [b] election of the following species for search purposes: [1] polymer resin is polystyrene (200-400 mesh, 1.23 mmol of OH per gram of resin; Example I); [2] linker is Wang resin (Example I); [3](a) preparation of compound (IVa) as defined in Example 2; (b) reaction of 4-nitrobenzaldehyde as defined in Example 3, first paragraph; and (c) delinker reaction with TFA to yield final product (I) as defined in Example 3 is acknowledged.

Applicants' traversal was made on the ground that no serious search burden exists for the Examiner, because [1] the inventions are not distinct as they are directed to the same inventive concept and [2] there is no undue search burden as restriction is not required.

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Applicants' arguments are found non-persuasive. The Examiner maintains that an undue search burden exists, because divergent searches requirements are required for Inventions II-VI. In particular, the inventions of Groups I-VI are [1] classified in different classification and subclassifications; Group I is classified in class 436, subclass 523, while Groups II -IV are classified in class 514, subclass 42 and Groups V and VI are classified in class 425, subclass 7.1; and [2] while Groups II-IV and Groups V-VI are classified, respectively in the same class and subclass, they are directed to different inventions of the inventive concept, which would require different and divergent searches of the patent and non-patent literature, as those respective inventions relate to different compounds, compositions and methods and processes involving different steps for different purposes. **The requirement is still deemed proper and is therefore made FINAL.**

6. Claims 10-15 are withdrawn from further consideration by the Examiner under 37 CFR 1.142(b), as being drawn to a non-elected inventions of Groups II-VI, the requirement traversed in Paper No. 6.

Claim Objections

7. Claims 1-9 are objected to because of the following informalities: improper language use of idiomatic English and grammatical errors. For the sake of clarity and conciseness, applicant is requested to review and amend the claim language to correct for idiomatic English and grammatical errors.

8. Appropriate correction of the above-identified issues is required.

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Specification

9. The disclosure is objected to because of the following informalities.
10. A reference to the prior application must be inserted as the first sentence of the specification of this application if applicant intends to rely on the filing date of the prior application under 35 U.S.C. 119(e) or 120. See 37 CFR 1.78(a). The above-identified application does not state the correct reference date of prior U.S. Provisional Application No. 60/061,619, filed October 9, 1997, now expired, under the specification heading entitled "Related Applications."
11. Appropriate correction of the above-identified issues are required.

Claim Rejections - 35 USC § 101

12. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.
13. Claims 1 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

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The preamble of the claim, which recites “a process using intermediates which are linked to a resin polymer for preparing chemical compounds of formula (I)” was interpreted as a “method of using.” Applicants are requested to amend the claim to delete the term “using intermediates which are linked to a resin polymer”, so that the claim 1 recites a “a process for preparing chemical compounds of formula (I).”

Claim Rejections - 35 USC § 112

14. The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15. Claims 1-9 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The omitted structural cooperative relationships relate to the fact that it is unclear from the claimed invention: [1] what the order, connection or attachment is for each of the elements, intermediates and/or components that form such intermediates that are used in the process steps to form a chemical compound of formula (I). In particular, [1] what is the connectivity or order of attachment of the individual atoms associated with individual or specific functional groups, which are utilized to form a specific intermediate (for example, in claim 1, group Y is defined as the functional group which is

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formed at the molecule of the formula (I); it is unclear how a functional group is formed at such a molecule of the formula (I); and [2] how are those respective intermediates are interlinked with each other in corresponding and subsequent reaction steps to form a compound of formula (I) of the claimed invention, etc. (for example, in step e of claim 1, it is unclear what reagents, other compounds, etc. a compound of (IV), (V) or (VI) or (VI)' or (V)' or (VI)' is reacted with to form a phosphorus-carbon bond to give compounds of the formulae (VII), (VIII) or (VII)' or (VIII)').

Therefore, the metes and bounds of the aforementioned claims cannot be determined as the specification, claims and the art do not recognize a defined set of compounds, active sites or screening methods that define the above-identified generic terms.

16. Claims 1-14 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

17. Claims 1-14 recites the term or limitation "the" to refer to specific terms throughout the body of those respective claims. There is insufficient antecedent basis for many of the corresponding terms in the aforementioned claims following the term or limitation "the." For example, in claim 1: the preamble recites the term "the formula (I)" and the terms, "the functional group" and "the molecule," are referred to in the definition of the element Y, but there was no antecedent basis for the use of those terms in the claim language preceding the recitation of those terms. While the Examiner has set forth below some of the terms that have insufficient antecedent

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basis, **applicant is requested to check all terms recited in the claims for [1] proper antecedent basis, especially those terms following the term or limitation “the”; and [2] amend the claim terms accordingly to reflect proper antecedent basis.**

18. Claim 1 is vague and indefinite for the recitation and/or have improper antecedent basis for each of the following terms identified below in sections [A]-[H]:

[A] in the definition section for elements of formula (I), the term:

- [1] R^1 is defined as “substituted” aromatic or heteroaromatic radical. It is unclear what substituents such aromatic or heteroaromatic radicals are substituted with;
- [2] R^2 is defined as an “organic radical . . . linked to the rest of the compound” and R^3 is defined as an organic radical . . . via a carbon atom.” The term organic radical identified in those phrases are vague, as it is unclear what definitions that term encompasses. For example, an organic radical may be interpreted to include many different organic functionalities. In the definition of R^3 , also it is unclear what the term “via” means and to what adjoining atom such an organic radical is connected “via” a carbon atom;
- [3] Y is “the functional group which is formed at the molecule of the formula (I)”; It is unclear what the term “functional group” and “formed at the molecule” refers to;

[B] in step a, the term:

- [4] [resin polymer] is defined with these terms that have insufficient antecedent basis: “the radical”, “the resin-linker compound”, “the n groups” and “the formula [linker-Z- E^1 - S^1]”;

[resin polymer] is further defined as the radical of a resin which “is connected via n binding sites.” It is unclear what the term “via” refers to in the preceding phrase.
- [5] Z is defined as a linker specific functional group or bond . . . after cleavage. . . from “the resin polymer linker radical. . .” There is insufficient antecedent basis for the term “the resin polymer linker radical. . .” It is also unclear as to what that term refers to.

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- [6] E' is defined as a "radical which is suitable for preparing R^1 . . ."; That term is vague and indefinite as it is unclear as to what such a term refers to, i.e., what makes such a radical "suitable" for preparing R^1 ;
- [7] S' is defined as a "functional group suitable" for palladium-catalyzed substitutions "analogous to the Heck reaction." It is unclear what the term a "functional group suitable" for palladium-catalyzed substitutions refers to. There is insufficient antecedent basis for the term "analogous to the Heck reaction."
- [8] n is defined with these terms that have insufficient antecedent basis: "the number"; "the functional groups [linker-Z-E¹-S¹]; "the resin"; and "the molecular weight".
- [9] on lines 12 -14 of page 51:
- [a] The following terms recited have insufficient antecedent basis: "the presence"; "the phosphinates (derivatives of hypophosphonic acid); "the formula (III)";
 - [b] It is unclear what the following terms refer to "a suitable palladium catalyst" and "the phosphinates (derivatives of hypophosphonic acid)". In the latter case, it is unclear whether the genus anticipates the species or the species anticipates the genus.
- [10] A is defined as "an organic radical"; The term "organic radical" is vague, as it is unclear what definitions that term encompasses. For example, an organic radical may be interpreted to include many different organic functionalities.
- [11] A* is defined as a group "which can be removed hydrolytically or after an intermediate reaction"; It is unclear what the term "which can be removed hydrolytically or after an intermediate reaction" refers to.
- [12] on lines 21-22 of page 51:
- It is unclear what the following terms refer to: "with substitution of the group S^1 to give a resin-bound compound of formula (IV): . . . [resin polymer]-[linker-Z-E¹-P(H)(=O)-O-A¹]_n. In particular, it is unclear as to what formula the term or group S^1 is being substituted into and how the vague definition of the term S^1 (provided on lines 7-8 on page 51) would result in a substitution of that term as "-P(H)(=O)-O-A¹" into formula (IV).

[C] in step b, term:

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[13] The following terms are vague and indefinite:

“derivatizing”; it is unclear as to how “compound (IV) is derivatized and to what constitutes such derivatives of that compounds; and

“in one or more further reaction steps”; it is unclear as what the term “in one or more further reaction steps” refers to.

[14] The following terms have insufficient antecedent basis: “the compound (IV)”; “the organic radical (E¹)’ ”; “the radical (E¹)’ ”; “the formula (IV)’ ”;

[D] in step c:

[15] The following terms are vague and indefinite:

“if appropriate” and a compound (V) or (V)’ “suitable for the resin bound synthesis”; it is unclear what those terms refer to.

[16] The following terms have insufficient antecedent basis: “the compound of the formula (IV) or (IV)’ ” and “the resin-bound synthesis”.

[E] in step d:

[17] The following terms is vague and indefinite:

“if appropriate”; it is unclear what that term refers to.

[18] The following terms have insufficient antecedent basis: “the compound (V) or (V)’ ” and “the compound (VI) or (VI)’ ”;

[F] in step e:

[19] The following terms are vague and indefinite:

“reacting” and “if appropriate”; it is unclear what those terms refer to.

[20] The following terms have insufficient antecedent basis: “the phosphonous acid or phosphonous ester group”; “the formulae (VII) or (VIII) or (VII)’ or (VIII)’”; “[resin polymer]-[linker-Z-(E¹)-P(E²)(=O)-O-A⁴]_n”; and “[resin polymer]-[linker-Z-(E¹)-P(E²)(=O)-O-A⁴]_n”;

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[21] on lines 32 of page 52:

The following term in the definition of E^2 is vague and indefinite: “an organic radical which can be derivatized to the radical R^2 .” The term “organic radical” in that phrase is vague, as it is unclear what definitions that term encompasses. For example, an organic radical may be interpreted to include many different organic functionalities.

The following term in the definition of E^2 has insufficient antecedent basis: “the radical R^2 .”

[G] in step f:

[22] The following terms are vague and indefinite: “modifying”; and “in such a manner”; it is unclear what those terms refer to.

[23] The following terms have insufficient antecedent basis: “the compounds”; “according to the abovementioned steps if required”; “the radicals E^1 , (E^1), E^2 and A^4 ”; “the resin bound compound”; and “the formula (IX)”.

[H] in step g:

[24] The following terms have insufficient antecedent basis: “the compound of the formula (I)”; “the resin-linker adduct”; “the formula (IX)”; and “the radicals[resin polymer].”

With respect to all of the above-identified terms in sections [A]-[H], the metes and bounds of the aforementioned claims cannot be determined as the specification, claims and the art do not recognize a defined set of compounds that define those generic terms.

19. Claim 2 is vague and indefinite for the recitation of the following terms: [1] R^1 is defined as phenylene which is unsubstituted or “substituted” or a heteroaromatic radical ...[which] is substituted or “unsubstituted”; [2] R^2 is defined as a hydrocarbon radical, which is unsubstituted

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or “substituted”; and [3] R^3 is defined as a hydrocarbon radical, which is unsubstituted or “substituted” or an aryl or heteroaryl radical, which is unsubstituted or “substituted.” In [1]-[3] above, it is unclear as to what is substituted on each of the terms R^1 , R^2 and R^3 , as it cannot be determined what substituents or group those terms “can be substituted” with.

Therefore, the metes and bounds of the aforementioned claims cannot be determined as the specification, claims and the art do not recognize a defined set of diseases, compounds or active sites that define the above-identified generic terms.

20. Claim 3 is vague and indefinite for the recitation of all the radicals that have the term unsubstituted or “substituted” preceding it; for example between lines 21-27 of page 54, the following terms are recited: “unsubstituted or “substituted” cycloalkyl, unsubstituted or “substituted” cycloalkenyl, unsubstituted or “substituted” aryl, unsubstituted or “substituted” heterocyclyl, unsubstituted or “substituted” cycloalkoxy . . . , etc. It is unclear as to what is substituted on each of those radicals defined in claim 3, as it cannot be determined what substituents or group those terms “can be substituted” with.

Therefore, the metes and bounds of the aforementioned claims cannot be determined as the specification, claims and the art do not recognize a defined set of diseases, compounds or active sites that define the above-identified generic terms.

21. Claim 4 is vague and indefinite for the recitation of the following terms: [1] for (R^2a), (R^2b), (R^2c), (R^2d) or (R^2e) and the corresponding chemical groups that appear next to the aforementioned terms; and [2] “ R^* and R^{**} together are an alkylene bridge”. It is unclear what

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those terms of [1] and [2] refer to, as it cannot be determined how those radicals and the corresponding terms relate to each other without a term to clarify the association between those terms (“wherein, (R²a) is a radical of formula -CHOH-R*..., etc” or that R* and R** form an alkylene bridge).

Claim 4 also is vague and indefinite for [3] the recitation in the definition of R* of all the radicals that have the term unsubstituted or “substituted” preceding it; for example between lines 19-25 of page 55, the following terms are recited: “unsubstituted or “substituted” cycloalkyl, unsubstituted or “substituted” cycloalkenyl, unsubstituted or “substituted” aryl, unsubstituted or “substituted” heterocyclyl, unsubstituted or “substituted” cycloalkoxy . . . , etc.; and [4] “an alkylene bridge which unsubstituted or “substituted by one or more radicals . . . selected from the group of substituents at the hydrocarbon radical for R*.” It is unclear as to what is substituted on each of those radicals defined in claim 4, as it cannot be determined what substituents or group those terms “can be substituted” with.

Therefore, the metes and bounds of the aforementioned claims cannot be determined as the specification, claims and the art do not recognize a defined set of diseases, compounds or active sites that define the above-identified generic terms.

22. Claim 8 is vague and indefinite in that it recites the term “an electrophile” associated with the variable “A⁴.” It is unclear what that term “electrophile” refers to, as the term “electrophile” may be interpreted to include many different organic chemical functionalities.

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Claim Rejections - 35 USC § 103

23. The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

24. Claims 1-9 are rejected under 35 U.S.C. § 103 (a) as being unpatentable over Schwabacher et al. (Synthesis, 1992, 1255-1260) in combination with Boyd et al. (Tetrahedron Lett., 1998, Vol. 37, No. 10, 1647-1650).

Schwabacher et al. teaches: [1] a method for the preparation of series of phosphinic acids and its corresponding derivatives, such as methyl esters of monoarylphosphinic acids, symmetrical and unsymmetrical diarylphosphinates, etc. that may be difficult to prepare by other routes; [2] which involves palladium catalyzed coupling of alkyl (aryl, etc.) iodides with methyl (or other substituted) phosphinate(s); [3] that such a method is compatible with various functional groups; that such derivatization or functional group manipulations may be achieved via conventionally known reaction chemistry (many example are given in this reference: for example phosphinic esters are generally prepared by esterification of the phosphinic acids with different reagents, such as trialkyl phosphite, by alcoholysis of an aryl or alkylidichlorophosphine or by Raney nickel reduction of a phosphothioate, aryl derivatives may be derived by organonmetallic reagents, such as Grignard reagent or aluminum trichloride, alkylphosphinic acids may be derived from

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phosphinic acid by radical addition to alkenes or from addition of phosphinic acid to a ketone or imine, etc., [4] wherein, phosphorus nucleophiles compatible with the process include: esters of alkyl and phenyl phosphinic acids, alkyl phenyl phosphine oxides, triphenyl phosphine and phosphonate esters; proceeds in reasonable yield despite thermal and hydrolytic sensitivity of methyl phosphinate; and [5] and that such compounds are useful as herbicide intermediates.

In view of the above, Schwabacher et al. *differs* from the claimed invention in that it *does not teach* [1] the formation of phosphinic acid compounds and its derivatives on a solid support resin; wherein [2] an organic starting material intermediate, such as an alkyl or aryl iodide is first anchored to the solid support resin, and [3] followed by the addition of the phosphorus containing intermediate leading to the formation of phosphonic acids and its corresponding derivatives..

However, Boyd teaches [1] the use of a resin for the multiple phase synthesis of phosphinic acid containing products on a resin.

Boyd et al. teaches: [1] the “first report of direct incorporation of phosphinic containing entities into a resin”; [2] that relates to multiple solid phase synthesis of aminophosphinic acids based on solid phase methodologies; wherein [3] an organic starting material, such as an aryl or an alkyl imine is resin bound forming an organic resin bound intermediate; [4] that resin bound intermediate is reacted with a phosphinate intermediate, BTSP (obtained by heating hexamethyldisilazane with ammonium phosphinate under inert atmosphere) which results in the resin bound 1-aminophosphinic acids (see, scheme 1, p. 1648) in which a nucleophilic addition and coupling results; [5] leading to the overall outcome of the synthetic strategy is the generation

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of a new phosphorus carbon bond by the addition of coupling reagent, BTSP, to resin bound aryl or alkylamines under very mild conditions; [6] to assess the purity and synthetic efficiency of this methodology, the formed phosphinic acid derivatives were selectively cleaved from the resin (using an acid hydrolysis) and isolated after standard workup procedures; [7] the above-identified method results in the high yield synthesis of a series of aliphatic and aromatic 1-aminophosphinic acid derivatives (see, Table I on p. 1649); [8] the main advantage of this solid phase methodology is that highly pure products can conveniently be prepared on a small scale in multiple reaction vessels; and [9] that such resin bound phosphino amino-acids and derivatives are (a) ripe for exploitation in the preparation of unique peptidomimetic combinatorial libraries; (b) modulate enzyme inhibitors, including therapeutic an angiotensin-converting enzyme (ACE), HIV protease and stromelysin-1 (MMP-3) inhibitor; (c) are suitable for further studies and potential incorporation into unique combinatorial chemical libraries that can be screened for potential biological activities; and (d)that novel synthetic procedures enable rapid preparation of structurally diverse aminophosphinic acid analogues of considerable use and interest.

A person of ordinary skill in the art would have been motivated to develop a method for the preparation of substituted phosphinic acids and its derivatives that may be difficult to make by other routes which involves palladium catalyzed coupling of aryl iodides with methyl phosphinate; because such compounds are useful as herbicide intermediates as taught by Schwabacher et al. and are ripe for exploitation in the preparation of unique peptidomimetic combinatorial libraries as such compounds have been shown to modulate enzyme inhibitors, including therapeutic an

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angiotensin-converting enzyme (ACE), HIV protease and stromelysin-1 (MMP-3) inhibitor and may have potential for incorporation into unique combinatorial chemical libraries that can be screened for potential biological activities and that novel synthetic procedures enable rapid preparation of structurally diverse aminophosphinic acid analogues of considerable use and interest as taught by Boyd et al.

In light of the foregoing, a person of ordinary skill in the art would have had a reasonable expectation of success such phosphinic acids and its corresponding derivatives because [1] Schwabacher et al. teaches a method for the preparation of methyl esters of monoarylphosphinic acids, symmetrical and unsymmetrical diarylphosphinates and their derivatives involving a palladium catalyzed coupling of alkyl, aryl, etc. iodides with phosphinates substituted with different substituent groups; and [2] Boyd et al. teaches: the “first report of direct incorporation of phosphinic containing entities into a resin” that relates to multiple solid phase synthesis of aminophosphinic acids based on solid phase methodologies which results in the resin bound 1-aminophosphinic acids or such phosphinic acid compounds cleaved from those solid supports.

It would have been *prima facie obvious* to a person of ordinary skill in the art at the time the invention was made to modify the teachings of Schwabacher et al. with the teachings of Boyd et al. to phosphine acids and its derivatives on solid support resins via a palladium catalyzed coupling reaction on a resin.

Status of Claims

25. No claims are allowed in the above-identified application.

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Conclusion

26. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Grace C. Hsu, Ph.D., J.D. whose telephone number is (703) 308-7005. The Examiner may be reached during normal business hours, Monday through Friday from 8:30 am to 6:00 pm (EST). A message may be left on the Examiner's voice mail.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Donald E. Adams, Ph.D., J.D., may be reached at (703) 305-0570. The fax number assigned to Group 1627 is (703) 305-4242. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1627 receptionist whose telephone number is (703) 308-0196.

Grace C. Hsu, Ph.D., J.D.

February 27, 2000

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BENNETT CELSA
PRIMARY EXAMINER

Bennett Celsa
2/27/00